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Patent Claims

1. Protein vaccine which comprises a mixture of viral protein molecules, **characterized in that** the molecules are sequence variants of a single viral protein or of part of same.
2. Protein vaccine according to claim 1, **characterized in that** the mixture contains  $\geq 10^2$  sequence variants.
3. Protein vaccine according to claim 2, **characterized in that** the mixture contains  $\geq 10^3$  and preferably  $\geq 10^4$  sequence variants.
4. Protein vaccine according to one of claims 1 to 3, **characterized in that** it comprises a mixture of GP120 proteins of HIV, which in each case differ from each other in their amino acid sequence in the region of the V2 loop and/or of the V3 loop.
5. DNA vaccine which codes for a mixture of structurally different virus proteins, **characterized in that** the vaccine contains a mixture of sequence variants of a viral DNA molecule or of part of same.
6. DNA vaccine according to claim 2, **characterized in that** it contains a mixture of DNA molecules which code for sequence variants of a viral protein or of part.

7. DNA vaccine according to claim 5 or 6, **characterized in that** the mixture contains  $\geq 10^2$  DNA molecules which differ from each other in their nucleic acid sequence.
8. DNA vaccine according to claim 7, **characterized in that** the mixture contains  $\geq 10^3$  and preferably  $\geq 10^4$  DNA molecules which differ from each other in their nucleic acid sequence.
9. DNA vaccine according to one of claims 5 to 8, **characterized in that** it codes for a mixture of structurally different GP120 proteins of HIV, in which the vaccine contains a mixture of DNA molecules, the nucleic acid sequences of which differ from each other in the region coding for the V2 loop and/or in the region coding for the V3 loop.
10. DNA vaccine according to claim 9, **characterized in that** it contains a mixture of DNA molecules which differ from each other in their nucleic acid sequence such that they code for a mixture of GP120 proteins which contain amino acid sequences which differ from each other in the V2 loop and/or in the V3 loop.
11. Nucleic acid sequence which is derived from the env sequence represented in SEQ ID NO: 1 or from a fragment of same, **characterized in that** it is modified such that it contains exclusively monovalent restriction sites.

12. Nucleic acid sequence according to claim 11,  
**characterized in that** the sequence is modified by the introduction of silent mutations.
13. Nucleic acid sequence according to claim 11 or 12,  
**characterized in that** it contains the sequence given in SEQ ID NO: 9.
14. Nucleic acid sequence, **characterized in that** it contains the sequence given in SEQ ID NO: 11.
15. Nucleic acid sequence, **characterized in that** it contains the sequence given in SEQ ID NO: 12.
16. Single-stranded nucleic acid sequence, which contain the region coding for the V3 loop and/or for the V2 loop of GP120, **characterized in that** in the V3 loop a 247 bp-long BglIII-XbaI fragment or a 283 bp-long BglIII-NheI fragment is exchanged for a modified fragment, and in the V2 loop a 139 bp-long PstI-BclI fragment or a 339 bp-long PstI-EcoRI fragment is exchanged for a modified fragment, the fragment/the fragments in each case containing inosine or a nucleic acid exchange at at least 6, preferably at 9 to 20 positions.
17. Single-stranded nucleic acid sequence which contains the region coding for the V2 loop and/or the region of GP120 coding for the V3 loop, **characterized in that** in the V3 loop a 247 bp-long BglIII-XbaI fragment or a 283 bp-long BglIII-NheI fragment is exchanged for a modified fragment, and in the V2 loop a 139 bp-long

PstI-BclI fragment or a 339 bp-long PstI-EcoRI fragment is exchanged for a modified fragment, the fragment/the fragments in each case containing a mutation at at least 6, preferably at 9 to 20 positions.

18. Double-stranded DNA which comprises hybrids of the single-stranded nucleic acid sequence according to claim 16 with the single-stranded nucleic acid sequence according to claim 17.
19. Nucleic acid mixture which comprises double-stranded DNAs, the nucleic acid sequences of which are derived from the env sequence in SEQ ID NO: 1 or SEQ ID NO: 11 or a fragment of same, **characterized in that** the nucleic acid sequences in each case differ from each other in the region coding for the V2 loop and/or in the region coding for the V3 loop.
20. Nucleic acid mixture according to claim 19, **characterized in that** the nucleic acid sequences differ from each other such that they code for a mixture of proteins which in each case contain amino acid sequences which differ from each other in the V2 loop and/or in the V3 loop.
21. Nucleic acid mixture according to claim 20, **characterized in that** the mixture contains  $\geq 10^2$  sequence variants.

22. Nucleic acid sequence according to claim 21,  
**characterized in that** the mixture contains  $\geq 10^3$  and preferably  $\geq 10^4$  sequence variants.
23. Protein mixture which comprises sequence variants of the GP120 protein, **characterized in that** it is mixture of proteins which contain amino acid sequences which in each case differ from each other in the V2 loop and/or in the V3 loop.
24. Protein mixture according to claim 23, **characterized in that** the mixture contains  $\geq 10^2$  sequence variants.
25. Protein mixture according to claim 24, **characterized in that** the mixture contains  $\geq 10^3$  and preferably  $\geq 10^4$  sequence variants.
26. Plasmid which contains an inserted double-stranded DNA according to claim 18.
27. Expression vector, **characterized in that** it contains an inserted nucleic acid sequence according to claims 11 to 15.
28. Expressions vector according to claim 27, **characterized in that** it contains the sequence given in SEQ ID NO: 10.
29. Expression vector, **characterized in that** it corresponds to DSM 12612.

30. Vector mixture which contains a mixture of plasmids according to claim 26, **characterized in that** the nucleic acid sequences of the plasmids differ in each case from each other in the region coding for the V2 loop and/or in the region coding for the V3 loop.
31. Vector mixture according to claim 30, **characterized in that** the mixture contains  $\geq 10^2$  plasmids which differ from each other in their nucleic acid sequence.
32. Vector mixture according to claim 31, **characterized in that** the mixture contains  $\geq 10^3$  and preferably  $\geq 10^4$  plasmids which differ from each other in their nucleic acid sequence.
33. Vector mixture according to one of claims 30 to 32, **characterized in that** the plasmids can be expressed in *E. coli* as host cells.
34. Vector mixture according to one of claims 30 to 32, **characterized in that** the plasmids can be expressed in eukaryotic cells, preferably in Cos, CHO or BHK cells, as host cells.
35. *E. coli* host cells which are transfected with a vector mixture according to claim 33.
36. Eukaryotic host cells which are transfected with a vector mixture according to claim 34.

37. Eukaryotic host cell according to claim 36, **characterized in that** they are a host cell from the group consisting of Cos, BHK or CHO cells.
38. Process for the preparation of the nucleic acid sequence according to claim 12, **characterized in that** so many silent mutations are introduced in a nucleic acid sequence coding for a viral protein that the obtained nucleic acid sequence still contains only monovalent restriction sites.
39. Process according to claim 38, **characterized in that** the nucleic acid sequence coding for a viral protein is the sequence according SEQ ID NO: 1 or SEQ ID NO: 11 or a fragment of same, into which so many silent mutations are introduced that it still contains only monovalent restriction sites.
40. Process for the preparation of the vector mixture according to claims 33 and 34, **characterized in that** plasmids, the nucleic acid sequences of which in each case differ from each other in the region coding for the V2 loop and/or in the region coding for the V3 loop, are ligated into a vector which can be expressed in host cells, preferably in *E. coli*, Cos, CHO or BHK cells.
41. Process for the preparation of the host cells according to claim 35 or 36, **characterized in that** the host cells are transformed with a vector mixture according to claims 30 to 32.

42. Process for the preparation of a protein vaccine according to one of claims 1 to 4, **characterized in that** the host cells are cultivated according to one of claims 35 to 37 under conditions which allow the expression of the mixture of viral protein sequence variants.
43. Process for the preparation of a DNA vaccine according to one of claims 5 to 10, **characterized in that** the process is carried out according to claim 40, the plasmids according to the invention being ligated into a vector which can be expressed in host cells of the organism to be vaccinated.
44. Use of a mixture of structurally different viral proteins which are sequence variants of a viral protein or of part of same, for the preparation of a vaccine for the prevention and/or therapy of a virus infection in humans.
45. Use of a protein mixture according to one of claims 23 to 25 for the preparation of a vaccine for the prevention and/or therapy of a HIV infection in humans.
46. Use of a mixture of DNA molecules which code for sequence variants of a viral protein or of part of same, for the preparation of a vaccine for the prevention and/or therapy of a virus infection in humans.



47. Use of a nucleic acid mixture according to claims 19 to 22 for the preparation of a vaccine for the prevention and/or therapy of a virus infection in humans.
48. Use of the nucleic acid mixture according to one of claims 19 to 22 for the preparation of a vector mixture according to one of claims 30 to 32 which can be expressed in host cells , the host cells being selected from the group consisting of *E. coli*, Cos, CHO and BHK cells.
49. Use of the vector mixture according to one of claims 30 to 32 for the expression of a protein mixture according to one of claims 23 to 25.
50. Use of the host cell according to one of claims 35 to 37 for the preparation of a protein mixture according to one of claims 23 to 25.
51. Pharmaceutical composition for the prevention and/or therapy of a virus infection, **characterized in that** it comprises a protein mixture and a nucleic acid mixture, the protein mixture comprising sequence variants of a viral protein or of part of same, and the nucleic acid mixture comprising DNA molecules which code for sequence variants of a viral protein or of part of same.
52. Pharmaceutical composition according to claim 51, **characterized in that** it comprises a protein mixture

according to claims 23 to 25 and a nucleic acid mixture according to claims 19 to 22.